Cystic Tumors of the Pancreas

New Clinical, Radiologic, and Pathologic Observations in 67 Patients

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Within a 12-year period we treated 67 patients (49 women, 18 men; mean age, 61 years) with cystic neoplasms of the pancreas, including 18 serous cystic adenomas, 15 benign mucinous cystic neoplasms, 27 mucinous cystadenocarcinomas, 3 papillary cystic tumors, 2 cystic islet cell tumors, and 2 cases of mucinous ductal ectasia. Mean tumor size was 6 cm (2 to 16 cm). In 39% the patients had no symptoms, and in 37% the lesions had been misdiagnosed as a pseudocyst. Computed tomography was useful for detection, for distinguishing the microcystic subgroup of serous cystadenoma, and for showing rim calcification (all 7 cases were malignant) but was not reliable for distinguishing neoplasm from pseudocyst, serous from mucinous tumors, or benign from malignant. Arteriography showed hypervascularity in 4 of 10 serous adenomas, 3 of 11 mucinous carcinomas, and 1 of 1 papillary cystic tumors. Endoscopic pancreatography showed no communication with the cyst cavity in 37 of 37 cases of cystic neoplasms but opacified the ectatic ducts in 2 of 2 cases of mucinous ductal ectasia. Stenosis or obstruction of the pancreatic duct indicated cancer. The tumor was resected by distal pancreatectomy in 25 patients, by proximal resection in 29, and by total pancreatectomy in one, with no operative deaths. Forty-four per cent of the tumors were malignant. In 10 cases the tumor was unresectable because of local extension or distant metastases, and those patients died at a mean of 4 months. Seventy-five per cent of those resected for cure are alive without evident recurrence. Because the epithelial lining of the tumor was partially (5% to 98%) absent in 40% to 72% of cases of the major tumor types, and the mucinous component comprised only about 65% of mucinous cystadenoma lining, misdiagnoses on frozen and even permanent sections were made. Mitoses and histologic solid growth correlated with malignancy. Neuroendocrine elements were seen in 87% of benign and 47% of malignant mucinous tumors. It is recommended that the terms macrocystic and microcystic be abandoned in favor of the histologic designations serous and mucinous. Incomplete examination of the cyst wall can be misleading, however. It is suggested that mucinous ductal ectasia be recognized separately from cystic tumors and that all of these lesions be resected, with the possible exception of asymptomatic confirmed serous cystadenomas.

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COMMON LORE CONCERNING cystic tumors of the pancreas is that they are rare,[1–8] potentially malignant,[3,5,6,8–10] but easily cured[5,7] or at least indolent,[3] and distinguishable from pseudocysts by biopsy of the cyst wall (which will show an epithelial lining).[4] Since the landmark papers of Compagno and Oertel in 1978,[2,3] it has been customary to distinguish microcystic (glycogen-rich serous) tumors from macrocystic (mucinous) tumors, a crucial point in that the former are universally benign[2,4,5] whereas the mucinous neoplasms all are frankly malignant or premalignant.[3,5,7,8–10] Since then there has been new recognition of two additional distinct entities, papillary cystic tumors[11–13] and mucinous ductal ectasia,[14,15] which probably have been erroneously included in earlier groupings. It also has been reported that computed tomographic (CT) scanning[16–18] and angiography[4,10,16,19] can differentiate between the microcystic and macrocystic varieties and that endoscopic pancreatography (ERCP) is not helpful in the differential diagnosis of cystic tumors from pseudocysts because even the tumors may communicate with the pancreatic duct.[20–22]

Despite the recent increased attention to pancreatic cystic neoplasms, there continues to be inadequate appreciation of the different types of cystic tumors and of the diagnostic and therapeutic approaches and pitfalls concerning them. As just one aspect of this, fully one third of the patients we see have been given the previous diagnosis of pseudocysts and many were inappropriately treated as a result.[23] In depicting our comprehensive experience with 'cystic tumors,' we will emphasize the difficulties in achieving a certain diagnosis without resection,

TABLE 1. *Criteria for Differential Diagnosis of Pancreatic Cystic Lesions*

Method	Finding
CT	Unilocularity *vs.* multilocularity, size of cysts, solid components, presence and form of calcification.
Angiography	Tumor vessels, hypervascularity vs. hypovascularity
ERCP	Communication with cystic element, pancreatic duct distortion or obstruction
Percutaneous aspiration	Cytology, amylase, CEA, CA 19-9
Cyst wall biopsy	Presence and type of epithelial lining

CT, computed tomography; ERCP, endoscopic pancreatography.

TABLE 2. *Pancreatic Cystic Tumors (Massachusetts General Hospital, 1978 to 1989)*

Histologic Diagnosis	No.
Serous cystadenoma	18
Mucinous cystic neoplasm	15
Mucinous cystadenocarcinoma	27
Papillary cystic tumor	3
Cystic islet cell tumor	2
Mucinous ductal ectasia	2
Pseudocyst	1

the dangers inherent in the malignancy of many of these tumors, and the opportunities for cure.

Materials and Methods

Sixty-eight patients with cystic lesions of the pancreas have been evaluated and treated by our group at the Massachusetts General Hospital in the last 12 years. Included were all patients found to have a cystic neoplasm or who were operated on and resected because of that presumed diagnosis. Excluded are all patients whose cystic lesions were known to be pseudocysts or that were determined to be pseudocysts before resection. In each case the clinical history was obtained from hospital and office records. The principal techniques and criteria used in differential diagnosis are summarized in Table 1.

All pathology specimens were reviewed by a single pathologist using three gross and 17 histologic variables. The diagnostic categories were designated as serous cystadenoma (glycogen-rich adenoma, 'microcystic' adenoma),[2,4,9,24,25] mucinous cystic neoplasm (mucinous cystadenoma, 'macrocystic' adenoma),[3,7-10] mucinous cystadenocarcinoma, papillary cystic tumor (papillary and cystic neoplasm, solid and papillary neoplasm),[11-13] cystic islet cell tumor,[26] mucinous ductal ectasia,[14,15] and pseudocyst.

Gross parameters included maximum transverse diameter, location, and loculation (unilocular or multilocular, size of loculations). Multiple hematoxylin and eosin-stained sections of each tumor were examined to estimate the percentage of the tumor cyst lining that was denuded of epithelium. The percentage of the remaining epithelium containing mucin-secreting cells was scored as 0, less than 25%, 25% to 75%, or more than 75%. Neuroendocrine components were confirmed by immunoperoxidase stains.

Results

There were 68 patients, 49 women and 19 men, with a mean age of 61 years. Fifteen patients (14 women) were younger than 50 years. Thirty-three tumors were located in the head of the pancreas and 35 in the body or tail. The histopathologic diagnoses are shown in Table 2. In 67 of 68 patients, the final diagnosis was neoplasm. The one pseudocyst was a 2-cm lesion in the pancreatic head of a patient with jaundice and no pain or history of pancreatitis or alcoholism.

Table 3 correlates the clinical characteristics with each tumor type. Note the general overlap of age groups, female predominance, and size and location of the various tumors. In most instances tumor type could not be discerned by gross appearance. Although many small (1 to 5 mm) loculations in a honeycomb or sponge pattern are characteristic of the microcystic form of serous cystadenoma, this accounted for only one fifth of these cases. In the rest of the serous cystadenomas and in all of the other tumors, the range of the loculation sizes was similar (1 to 16 cm) and was not a distinguishing feature. Thirty-nine per cent of patients with benign lesions had no symptoms; their tumors were found incidentally because of a palpable mass or on a scan performed for other purposes. Two of 38

TABLE 3. *Clinical Characteristics of Pancreatic Cystic Tumors*

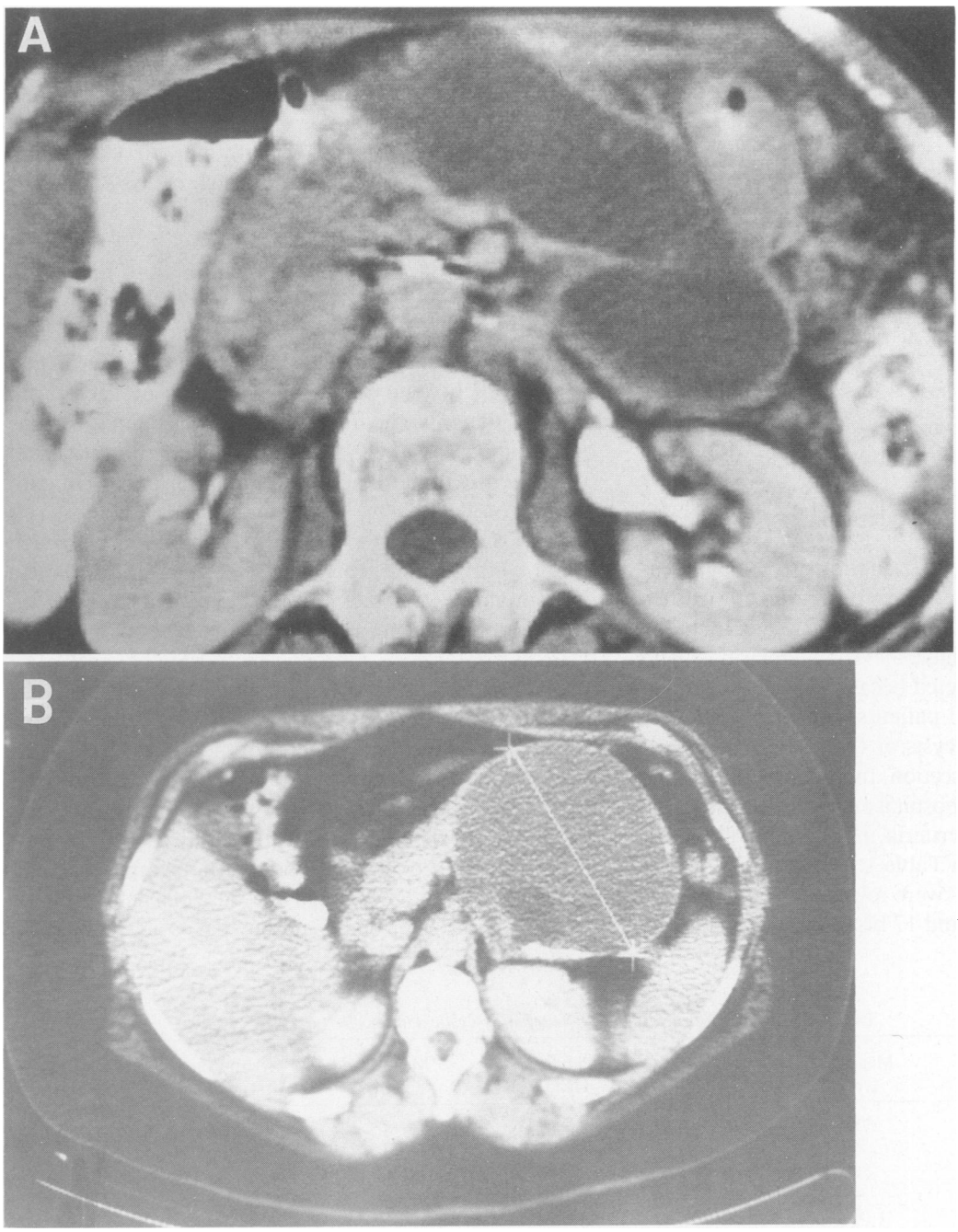
Type	Mean Age (years)	Female (%)	Pancreatic Head (%)	Mean Size (cm)	Symptoms (%)	Pseudocyst mis-dx (%)
Serous cystadenoma	64	72	39	5	56	33
Mucinous cystic neoplasm	59	81	47	5	60	40
Mucinous cystadenocarcinoma	63	74	56	6	85	41
Papillary cystic tumor	44	67	13	8	67	33
Cystic islet cell tumor	60	50	0	5	50	0
Mucinous ductal ectasia	69	0	100	6	100	50

benign tumors presented with jaundice and three with pancreatitis. Among 30 patients with malignant tumors, only 15% were not symptomatic, and five presented with jaundice.

In 13 instances the patient also had a separate cancer concurrently or previously. Those were located in the pancreas (2), bile duct (1), urogenital tract (6), or other locations (4).

In 25 cases the patient had been assigned a diagnosis of pseudocyst. This resulted in cyst-enteric anastomoses (7 cases), percutaneous needle or catheter drainage (4 cases), and prolonged observation for 1 to 8 years. In four cases tumor that was resectable (but not resected) at first operation was metastatic and unresectable at reoperation.

Computed tomographic and ultrasound scans, performed in 65 cases, were excellent tools for detection of cystic tumors. At least 15 cases were identified because of incidental discovery on scans performed for other reasons. Loculations often were detectable but frequently were inapparent when the septae were delicate. The pres-

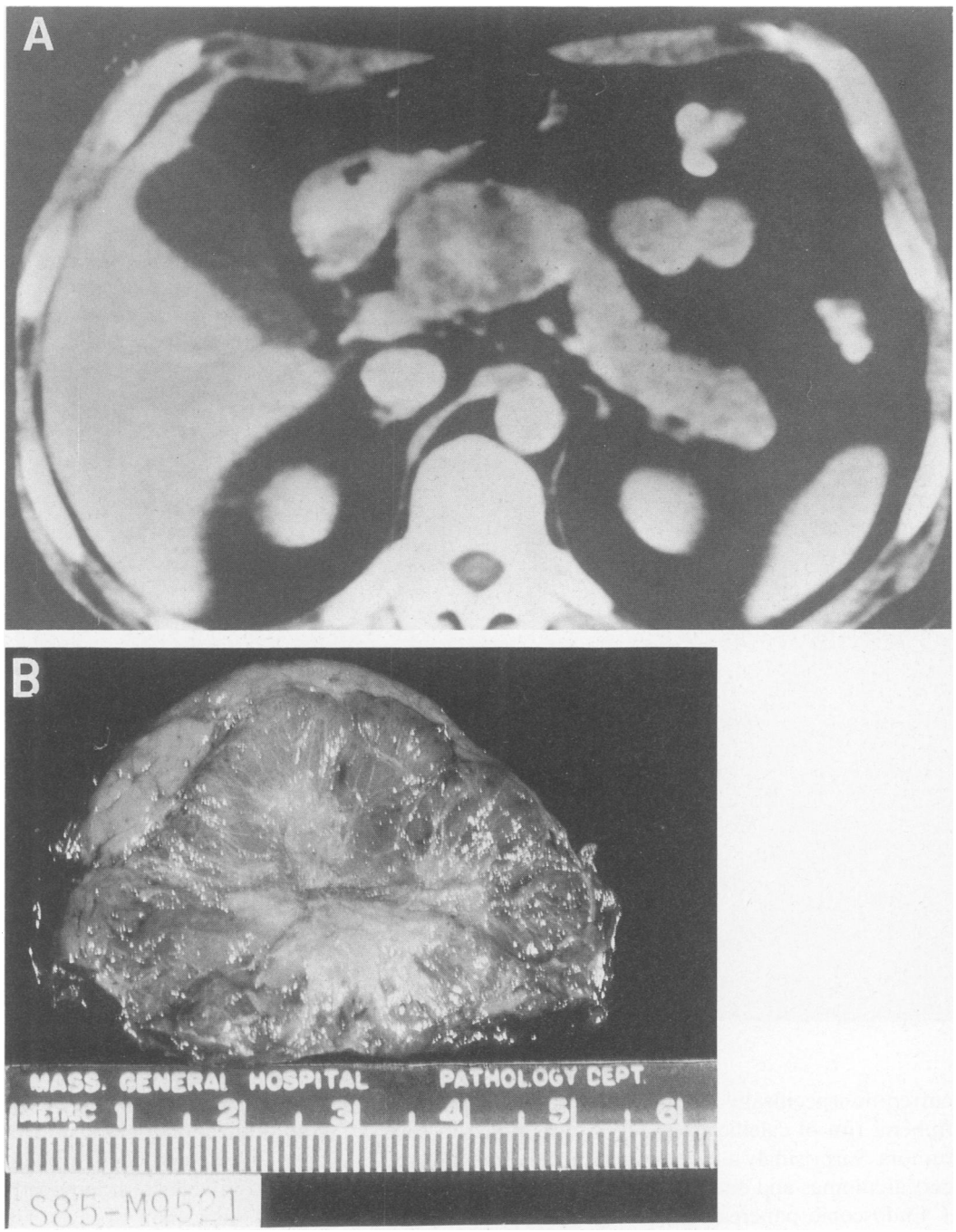


FIGS. 1A and B. Computed tomographic scans showing two serous cystadenomas, one with a septum (A) and one that appears to be unilocular (B).

ence of loculations proved to be a reliable criterion for neoplasm (as opposed to pseudocyst) but were unreliable for differentiating serous from mucinous tumors (Fig. 1). So-called microcystic adenomas (all serous) were identifiable by CT when multiple small loculations were apparent, but this occurred in only 50% of serous cystadenomas. The central scar and sunburst calcification, which are said to be highly suggestive of microcystic adenomas, were seen in only 2 of 18 cases (Fig. 2).

A solid component to the tumor was identifiable in some instances but not in others (Fig. 3). Often the solid components were too small to be resolved by CT. Unless there was considerable solid tumor (Fig. 4) or liver metastases, CT was ineffective in distinguishing benign from malignant macrocystic lesions. An estimation of local resectability could be made with fair reliability, but liver and peritoneal metastases were missed in five cases.

Localized calcifications were common (30%) and oc-



FIGS. 2A and B. Computed tomographic scan showing a central sunburst calcification (A), correlating with the central scar in a microcystic adenoma (B).

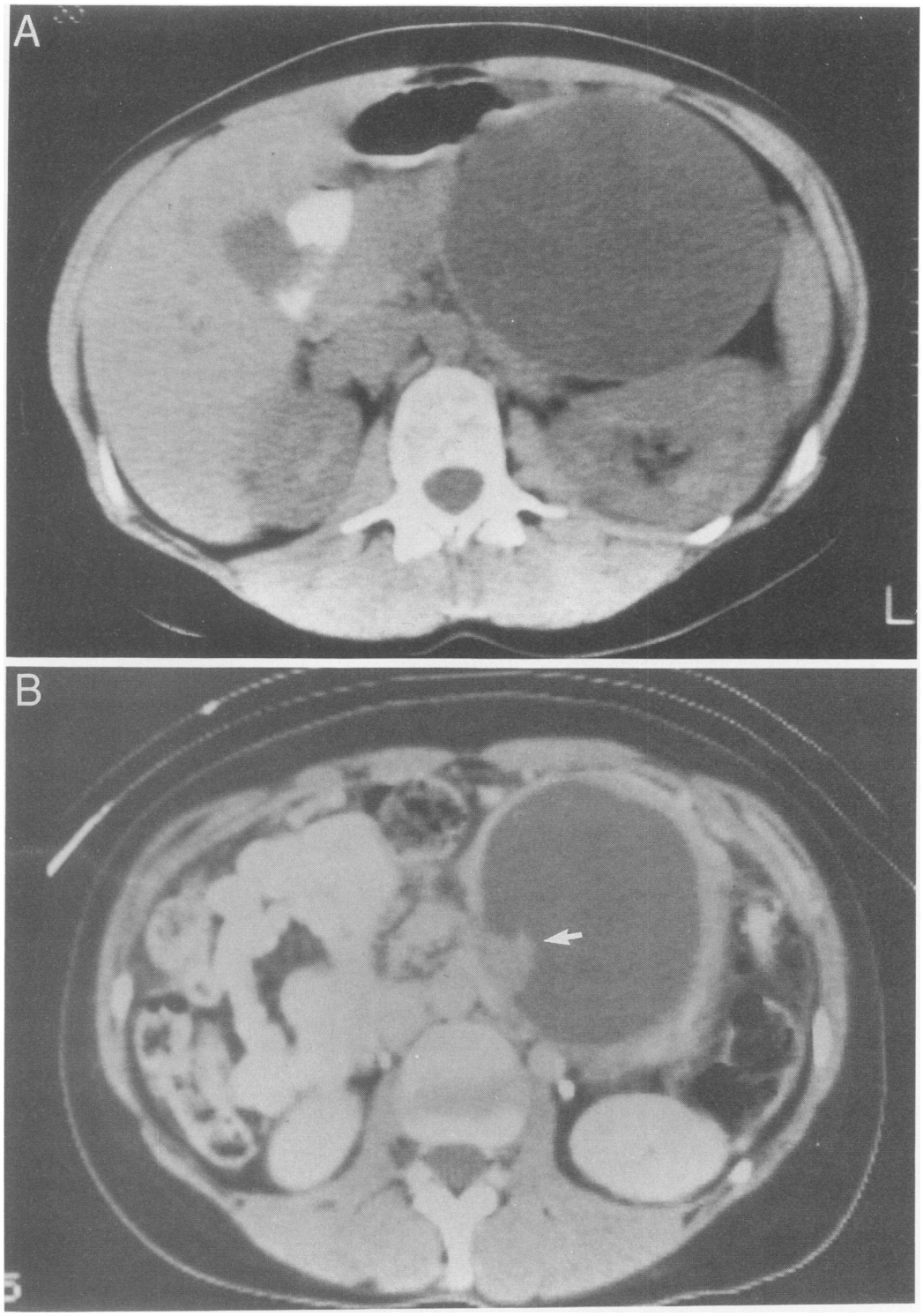


FIG. 3. Computed tomographic scans of two mucinous cystadenocarcinomas. Solid excrescences were present within the cyst cavities of both but were visible on scan in only one (arrow).

curred nonspecifically in each of the tumor types. A peripheral rim of calcification (Fig. 5) was noted in seven tumors. Surprisingly all were cancerous: six mucinous adenocarcinomas and one malignant papillary cystic tumor.

Endoscopic pancreatography (ERCP) was performed in 40 cases (Table 4). In 38 of 40 patients there was no communication demonstrated between the pancreatic duct and the cyst cavity (including the pseudocyst). Distortion of the duct (draping or bowing over a large tumor) (Fig. 6) was seen in 14 cases. Three ducts were constricted

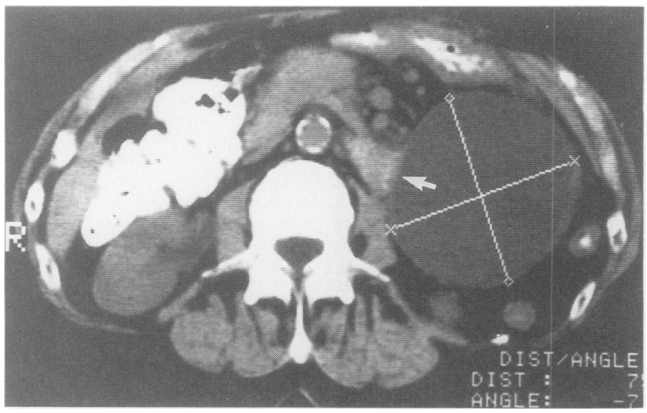


FIG. 4. Computed tomographic scan of an unresectable mucinous cystadenocarcinoma. A component of solid tumor is seen to the left of the cyst (arrow). Cytologic examination of a percutaneous aspirate showed malignant cells.

and four ducts were completely obstructed (Fig. 7) among 17 cancers.

Celiac and superior mesenteric angiography was performed in 27 cases. Hypovascularity (negative impression due to splaying of vessels) was seen in 19 cases. Hypervascularity (said to be characteristic of microcystic adenomas) was present in only 4 of 10 serous cystadenomas (Fig. 8), and was also seen in 3 of 11 mucinous adenocarcinomas and 1 islet cell tumor (Table 5).

Aspiration of the cyst cavity was performed too infrequently to make broad comments. In six of six cases, the amylase content was low. In four mucinous tumors, mucinous cells were identified on cytologic study and two of those had cytologic characteristics of malignancy.

Operations were performed on 65 patients: 25 distal (body and tail) resections, 29 proximal pancreatoduodenectomies, 1 total pancreatectomy, and 10 explorations with biopsy of cancer unresectable because of local extension (9) or distant metastases (6). There were no postoperative deaths. One patient with a postoperative infected mucinous fistula was not fit for reoperation after a previous cyst duodenostomy, and two are awaiting operation. Noteworthy was a marked desmoplastic response seen around the tumor in a number of instances. This dense fibrotic reaction made separation of the lesion from surrounding structures, such as the mesocolon, colon, and duodenum, very difficult and raised concerns about invasive cancer. In one case the transverse colon was removed with the tumor on this account. Unless there were metastases or grossly invasive cancer, usually it was impossible for the surgeon to distinguish between tumor types or to determine whether the tumor was malignant (Fig. 9).

The distribution of histopathologic diagnoses is shown in Table 2. Note from Table 3 that the mean cystic tumor size is the same in all groups but also that there is overlap at all points on the spectrum of loculation size. Both serous and mucinous cysts ranged in size from 2 to 16 cm and could be unilocular or multilocular. Similarly the ranges of benign and malignant cysts are similar. Only the microcystic honeycomb pattern was purely serous.

Histologic examination (Table 6) showed an incomplete (denuded) epithelium in 40% of serous cystadenomas and 72% of mucinous tumors (benign or malignant). The area of absent epithelium averaged 40% of the wall (up to 98%) in the denuded tumors. This phenomenon led directly to errors in diagnosis on microscopic examination of both frozen and permanent sections until the entire specimen was examined on review.

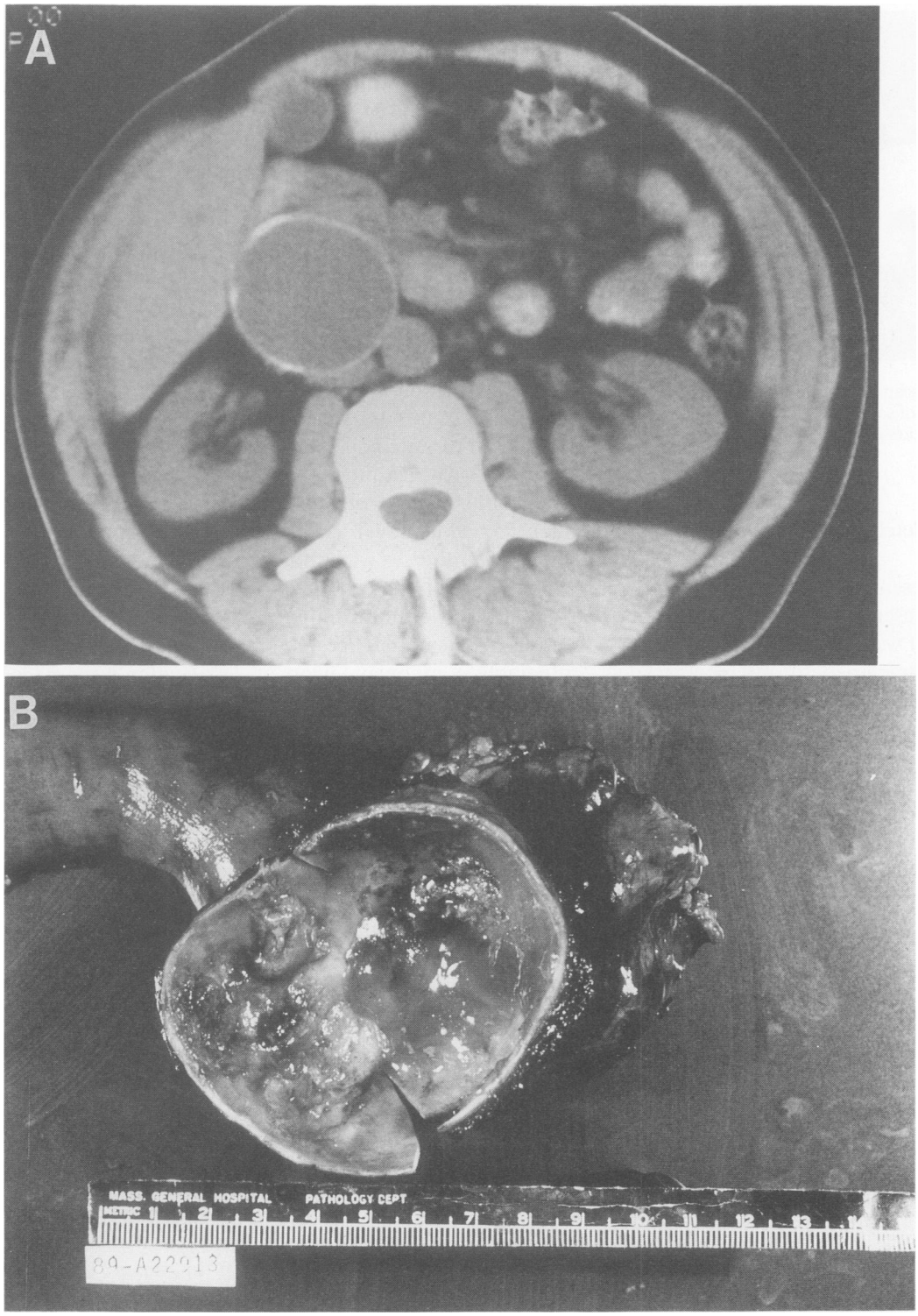
Mucinous tumors were found not to be uniformly composed of mucinous epithelium. Among benign mucinous neoplasms, mucinous epithelium covered an average of about 65% of wall area (67% of cases were less than 75% mucinous). Among malignant mucinous tumors, 89% of cases were more than 75% mucinous. Mucinous epithelium accounted for 25% to 75% of all three papillary cystic tumor linings but was not found in any serous cystadenoma. Because of the nonuniformity of the mucinous component, errors of classification were made on initial examination in three cases.

Neuroendocrine cells were noted (and confirmed by immunoperoxidase stains) in 87% of mucinous cystic neoplasms and 47% of mucinous cystadenocarcinomas (and in all three islet cell tumors, of course). An endocrinopathy was apparent in only one patient, who had a duodenal gastrinoma along with a serous cystadenoma of the pancreatic body.

Mitoses were found in 88% of mucinous cystadenocarcinomas, in one of two malignant papillary cystic tumors, and in the malignant mucinous ductal ectasia. No mitoses were found in any serous cystadenoma or in any benign mucinous cystic neoplasm.

Histologic solid growth (foci in which cells piled up in 'solid' fashion without individual cell contact with the basement membrane) was not found in any serous cystadenoma but was present in all of the other tumor varieties. In the mucinous series, solid growth was present in 8% of benign tumors and in 88% of malignant tumors.

Clinical and histopathologic evidence of malignancy was found in 44% of the tumors in this series (Table 6). This occurred in 27 of 42 of the mucinous series, 2 of 3 of the papillary cystic tumors, 1 of 2 of the mucinous ductal ectasia, and in none of the serous cystadenomas. We expect that some islet cell tumors will be malignant, but the sample size (2) in this collection is small. Only 63% of the mucinous adenocarcinomas were judged to be clearly resectable. Of the latter one patient had a positive resection margin (and died of cancer) and another



FIGS. 5A and B. Computed tomographic scan showing calcification of the rim of a pancreatic cyst (A). Despite the apparently smooth walls, the opened specimen contained excrescences of carcinoma (B).

had a positive adjacent lymph node (and remains free of disease at 2 years). Overall 13 of 17 resectable mucinous cancer patients (76%) are alive without evident recurrence (48% of all mucinous cancers) at 6 months to 10 years. All deaths in the group resected for cure occurred within 15 months of resection. Twenty-two per cent of the mucinous cystadenocarcinomas had nonlocal metastases. All patients with unresectable local or metastatic cancer died at an average of 4 months. The man patient with papillary cystic carcinoma died with recurrence at 4 years, but the

TABLE 4. *Endoscopic Pancreatography in Pancreatic Cystic Tumors*

Type	No.	Communicating	Draped	Constricted	Obstructed
Serous cystadenoma	8	0	4	0	0
Mucinous cystic neoplasm	9	0	6	0	0
Mucinous cystadenocarcinoma	17	0	3	3	4
Papillary cystic tumor	3	0	0	0	0
Mucinous ductal ectasia	2	2	2	0	0
Total	39	2	15	3	4

woman is well at 5 years. The mucinous ductal ectasia contained an *in situ* cancer and the patient is well.

Discussion

Cystic neoplasms of the pancreas are thought to be rare, perhaps accounting for 10% to 13% of 'pancreatic cysts' and 1% of pancreatic cancers.[1,27] Our experience indicates a far greater frequency, which was partly influenced by the concentration of cases at our institution but also due to corrected identification of neoplasms previously diagnosed as pseudocysts. The differential diagnosis of a cystic lesion of the pancreas must include a variety of neoplasms, particularly in the absence of antecedent factors or events that could generate a pseudocyst. Irregularity or loculation in the cyst or a solid component when present indicate a tumor, but their absence on scan is not unusual.[4,17] Failure to be alert to the possible presence of tumors, especially in young women, too often leads to errors in treatment.[23,26] Mucinous cystic neoplasms of the pancreas are likely to develop in patients with Von Hippel-Lindau disease.[4,28]

While identification of a cystic tumor is relatively easy (we included only one pseudocyst erroneously in our preoperative diagnoses in this series) the identification of the specific tumor type may be difficult because of overlapping of characteristics: most occur in middle-aged women (14 younger than 50 years), have a mean diameter of 5 to 6 cm, and may present with pain, pancreatitis, or no signs. To the six species of tumor found in the present series could be added lymphangiomas, hemangiomas, and high-grade ductal cancers that can partially liquefy because of central necrosis.

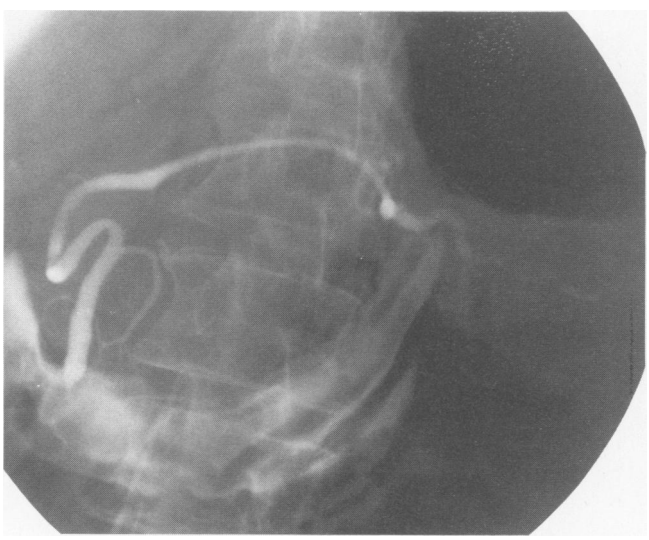


FIG. 6. Endoscopic pancreatogram showing distortion of the pancreatic duct by a tumor over which it is draped.

Certain physical characteristics proved helpful in diagnosis. Whereas size and location of the lesion were of no value, loculation and solid components on scan are reliable indices of neoplasm. The appearance of a loculated neoplasm generally differs from that of multiple pseudocysts in that the septae are more delicate, the cysts more coalescent, and the locules often irregular in shape.[16-18] Calcification is common in cystic tumors[16,18] but we have not seen it in the wall of pseudocysts, albeit calcifications in the pancreas are commonplace in chronic pancreatitis. Calcification of the rim of the cyst wall,[13,16] either as a crescent or as a complete circle, was seen in seven cases; to our surprise all were malignant. This phenomenon perhaps attests to the long natural history of some cystic tumors, especially those undergoing malignant degeneration. The central 'sunburst' calcification of some serous cystadenomas is characteristic and highly suggestive of that particular entity[16] but occurred in only 11% of our cases and has been said to be exceptional.[17,29] Hypervascularity on arteriographic examination indicates a neoplasm, but not its type. While said to be characteristic of the 'microcystic adenoma,'[19,29] we found that to be true in only 40% of serous cystadenomas and also to occur in 33% of mucinous adenocarcinomas.

Endoscopic pancreatography was helpful primarily in indicating some cases of cancer. In 50% of all studies the pancreatogram was normal; in 33% there was nonspecific bowing around the mass; but in cancers there was stenosis or occlusion in 18% and 24%, respectively.

It has been suggested that pancreatography could be useful in distinguishing cystic tumors from pseudocysts in that the pancreatic duct can be shown to communicate with 70% of pseudocysts,[30] but a neoplastic cyst ought to

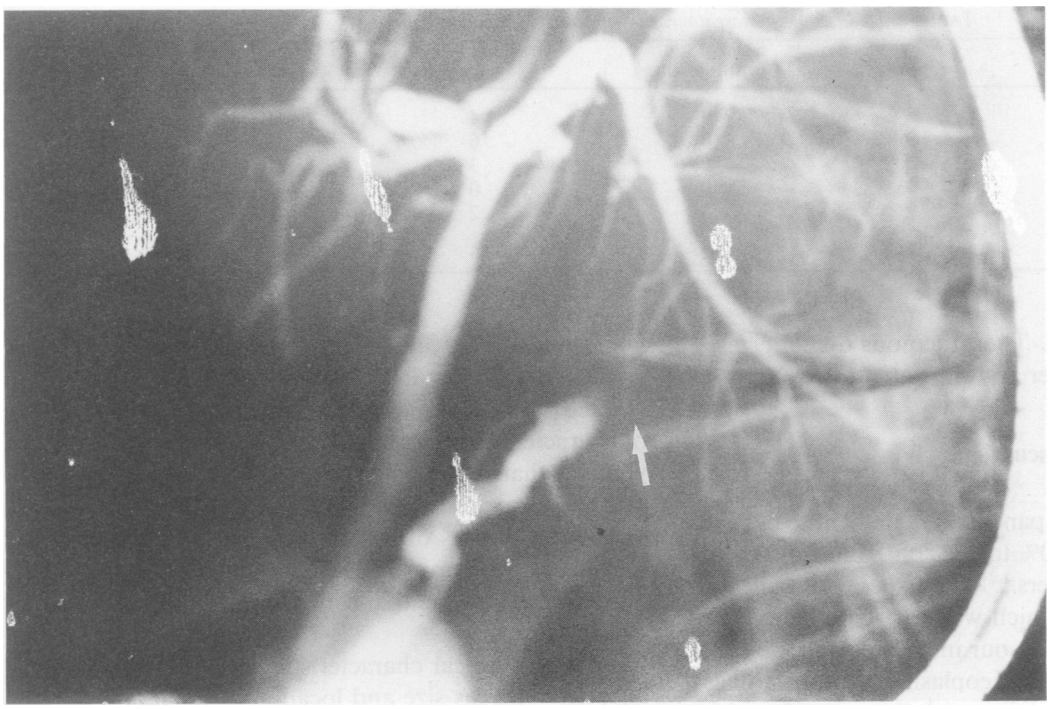


FIG. 7. Endoscopic pancreatogram showing complete obstruction of the pancreatic duct (arrow) by a mucinous cystadenocarcinoma. The biliary tree is also opacified.

be separate.[23] Although there are a few anecdotal reports of single examples of opacification of a cystic tumor at ERCP,[20–22] most reports are of absence of communication, and we had no instance of communication in pancreatograms performed in 37 patients with neoplastic cysts. Other than the possibility that an occasional neoplastic cyst may have a communication with the pancreatic duct, we suggest two possible alternative explanations for the previously reported observations: (1) the cavity filled at pancreatography was, in fact, an associated pseudocyst

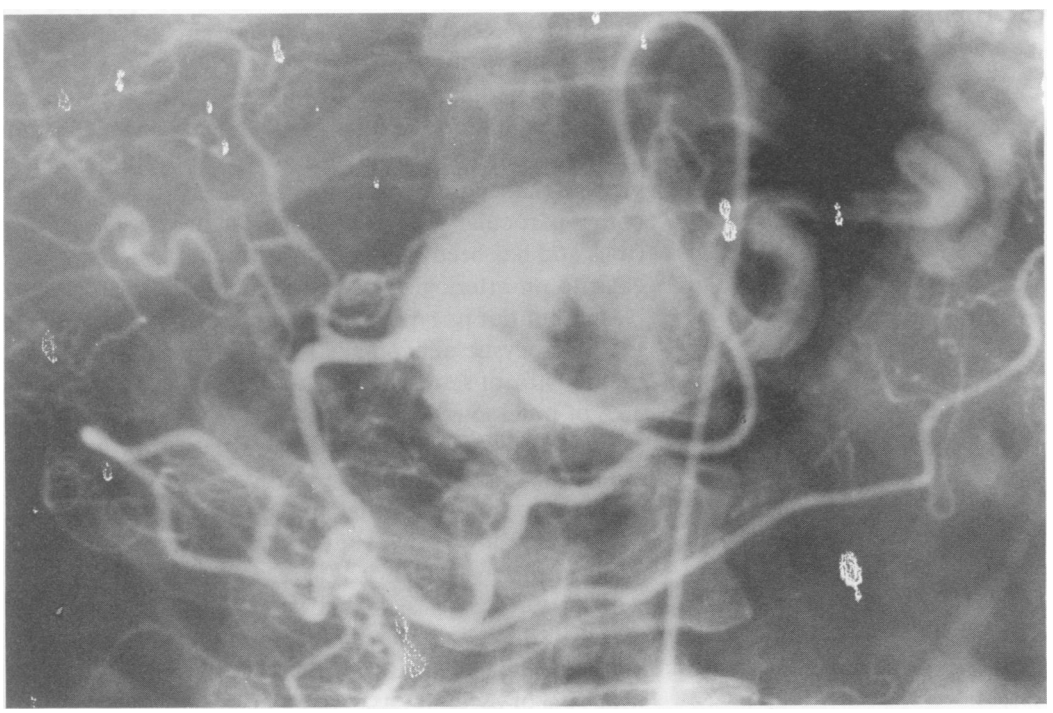


FIG. 8. Celiac arteriogram showing a hypervascular serous cystadenoma (same patient shown in Figure 2).

TABLE 5. *Angiography in Pancreatic Cystic Tumors*

Type	No.	Hypervascular	%
Serous cystadenoma	10	4	40
Mucinous cystic neoplasm	6	0	0
Mucinous cystadenocarcinoma	11	3	27
Cystic islet cell tumor	1	1	100
Mucinous ductal ectasia	2	0	0
(Pseudocyst)	1	0	0

arising as a consequence of obstructive pancreatitis caused by the underlying cystic tumors; and (2) the lesion studied was an example of mucinous ductal ectasia, rather than cystadenoma.

Mucinous ductal ectasia is a newly recognized premalignant lesion[14,15] in which there are papillary hyperplasia and mucin overproduction along the pancreatic duct, involving part or all of the gland and leading to obstructive pancreatitis because of mucus filling the duct. A startling experience for the endoscopist may be to see mucus exuding through the ampullary orifice[14,15] (as seen in one of our cases). Pancreatography shows filling of the dilated 'cystified' ducts along with the intraluminal mucus globs. It is clear that some previous reports have unknowingly included mucinous ductal ectasia cases among cystadenomas[10] and that the current literature continues to confuse the two entities,[15] which are entirely different clinically and morphologically.

Percutaneous aspiration of cystic tumors for sampling of amylase content,[23,31] CEA[32,33] or CA 19-9[34] level, and cytologic examination[10,35,36] has been reported sporadically. The number of cases is far too small to evaluate how sensitive or reliable these parameters might be. Our own sparse experience suggests that amylase content of neoplastic cysts is low (six instances)—there are two single case reports to the contrary[20,22]—and that cytologic examination of the aspirates may show mucinous cells or cytologically malignant cells (one case each). Percutaneous sampling of the cyst fluid deserves further consideration, limited mainly by the concern that malignant cells could potentially be spilled and seeded.

The irregularity of the tumor cyst epithelium is a prominent feature of many of these tumors[3] and merits a strong caveat. It occurred in 40% of the serous cystadenomas and 72% of the mucinous tumors and involved an average of 40% (up to 98%) of the cyst wall area. In fact this led to initial diagnoses as pseudocysts in four cases, errors that were corrected only with careful review of additional tissue sections from other areas of the tumor. It seems very likely that others have also fallen into this trap. Of incidental note, we wonder whether the intense desmoplastic response found around some mucinous neoplasms might be caused by transmural passage of irritating cyst contents through areas of cyst wall without an epithelial barrier.

Similarly the mixed nature of the epithelium of the mucinous tumors could lead to errors in diagnosis. Whereas the serous cystadenomas had uniform serous epithelium, the benign mucinous neoplasm contained an average of 65% mucin-producing cells (as little as 5%), but most of the other cells were serous. Nonetheless it is the mucinous component that is the important determinant because malignant degeneration occurred only in this portion. In tumors containing both benign serous and mucinous areas, cancer was seen to arise always from the latter. Because the gross appearance of most of the cystic tumors is generally similar and, with the exception of the microcystic variety of serous cystadenoma, loculation size may not be different, the diagnostic impression of the surgeon is also subject to error.

It is believed that the duct cell is the progenitor of mucinous neoplasms of the pancreas.[9,27] Because the neuroendocrine cells of the pancreas are now thought to have a similar origin, it is not surprising to find neuroendocrine-type cells in so many of the mucinous tumors.[37] Our studies with immunoperoxidase stains for specific hormones will be presented elsewhere, but there was no clinical evidence of endocrinopathy in these patients, with the exception of one who has a simultaneous duodenal gastrinoma. Whether the cystic islet cell tumors should be considered true relatives of the mucinous cystic neoplasms is undetermined.

Generally it is accepted that pancreatic cystic tumors with serous epithelium are not and do not become malignant[2,4,8,9] but that all of the other cystic tumors are either malignant or have the potential for malignant degeneration.[3,4,5,7-15] Compagno and Oertel[3] emphasized the difficulty of the histopathologic diagnoses of malignancy in the absence of local invasion or overt metastases. We

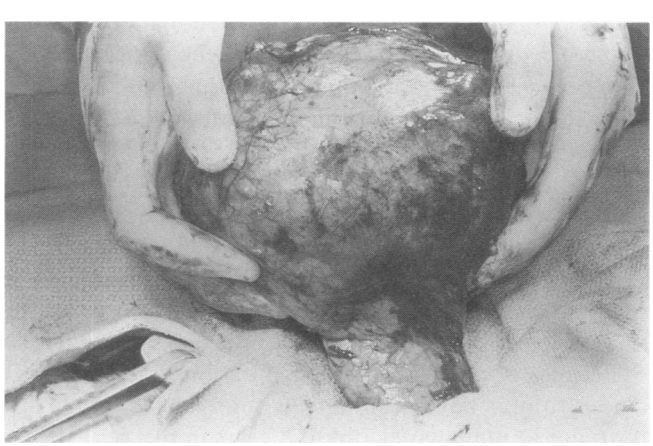


FIG. 9. Serous cystadenoma of the tail of the pancreas (same patient shown in Figure 1).

TABLE 6. *Histopathologic Findings in Pancreatic Cystic Tumors (% of total in group)*

Type	Calcification	Rim Calcification	Denuded	Neuroendocrine Elements	Mitoses	Solid Growth
Serous cystadenoma	30	0	22	0	0	0
Mucinous cystic neoplasm	13	0	75	87	0	8
Mucinous cystadenocarcinoma	33	22	69	47	88	89
Papillary cystic tumor	67	33	0	0	33	100
Cystic islet cell tumor	0	0	0	100	0	100
Mucinous ductal ectasia	100	0	0	0	50	100

have found mitoses in 84% of known malignant tumors and in none of the apparently benign tumors. The histologic characteristic of solid tumor cells growth (cells piled up without contact with the basement membrane) was almost as reliable an index because it was found in 88% of mucinous cystadenocarcinomas but also in 8% of otherwise benign mucinous cystic neoplasms. It is possible that solid growth is a histologic index of incipient or early malignancy.

It is frequently stated that cystadenocarcinomas of the pancreas are highly curable.[3,5,7,9] Most are said to be resectable,[7,8] and cure rates of 70% are quoted for mucinous cystadenocarcinoma.[7,8] Remine et al.[6] of the Lahey Clinic pointed out that the widely cited series from the Mayo Clinic reported by Hodgkinson et al.[7] contained a disproportionate number of low-grade tumors (20 pf 21 were grade 1 or 2). In their own study Remine et al.[6] found that 8 of 11 patients with mucinous cystadenocarcinoma had a highly dysplastic aggressive cancer and already had metastases at the time of operation. Their findings implied two distinct populations of mucinous cancers: those with good tumors (none of these patients died of cancer when the lesion was curatively resected) and bad tumors (eight patients with metastases died rapidly). The latter contradicts the wildly accepted statement by Compagno and Oertel[3] that the prognosis of unresectable mucinous adenocarcinoma is substantially better than that of the usual noncystic ductal adenocarcinoma of the pancreas. Our own experience supports that of the Lahey Clinic group. Sixty-four per cent of our mucinous tumors were malignant and 33% already had metastases; only 63% were resectable. Of those resected for intended cure, 76% are currently alive without evident recurrence (48% overall). Of those not resected or incompletely resected, all have died within a time frame similar to that of other pancreatic cancers (average, 4 months). In addition there may be an increased frequency of other cancers in these patients.[8]

Because of the extraordinary duration that some mucinous tumors have been 'safely' observed before the appearance of malignancy (up to 8 years in this series), it is accepted generally that all mucinous cystic neoplasms should be considered potentially malignant.[3-6,9] Our observations suggest that mucinous cystic neoplasms may be relatively dormant for years in a state of latent malignancy[3,38] but have the capacity to convert to high-grade aggressive cancer without warning. For these reasons, even if asymptomatic (as so many of our patients were), all mucinous cystic neoplasms should be resected: neither observation nor cyst-enteric anastomosis[6,20,23] are logical or acceptable alternatives.

Consistent with other reports, our experience with papillary cystic tumors[11-13] and mucinous ductal ectasia[14,15] suggests that these tumors frequently are malignant but are likely to be resectable and curable, despite impressive size. In two cases of papillary cystic cancers, metastases to the liver and omentum were also resected with resulting cure.[13,39]

From this experience we conclude that the cystic neoplasms of the pancreas include a variety of tumors, benign and malignant. These have shared clinical and radiologic characteristics that make preoperative distinction difficult, with the exception perhaps of the true microcystic subgroup of serous cystadenomas. In most cases it is not possible prospectively to separate with confidence the serous cystadenoma (always benign) from mucinous neoplasms (always malignant or potentially malignant). We strongly recommend that the terms microcystic and macrocystic be discarded as inaccurate and misleading, and that the exact histologic designations (serous and mucinous) be used. This means that the exact diagnosis in many cases cannot be made until the full specimen is available for study. Even at that time gross inspection and biopsy (or anything less than full histologic evaluation of multiple areas of the cyst walls) can be misleading for distinguishing pseudocysts from neoplasm, serous from mucinous, and benign from malignant.

Mucinous ductal ectasia should be recognized as a separate entity, clearly different from mucinous cystic neoplasms, arising within the pancreatic ducts rather than separate from them, and causing mucinous obturation of the pancreatic ducts with resulting obstructive pancreatitis and gland failure.[14,15] Endoscopic pancreatograms in mucinous ductal ectasia uniformly show filling of the ectatic ducts, whereas in our experience none of the 37 pancrea-

tograms (or any of the examinations by a pathologist) showed communication between the pancreatic ducts and the cystic structures of the other tumors.

We recommend that cystic tumors of the pancreas should, in general, be resected for the relief of symptoms and for treatment of cancer. Some authors suggest that asymptomatic serous cystadenomas—the only cystic tumor that has never been malignant—can be observed safely, especially in elderly or poor-risk patients.[2,8,24] While this concept is theoretically reasonable, in practice it is difficult to determine with certainty that a given lesion is a serous cystadenoma and not one of the other, more ominous varieties. We suggest that the option of nonintervention may be safe only in those tumors that have the CT characteristics of microlocularity and the central scar with sunburst calcification. Otherwise, given the low risk of resection, it is safer to remove the neoplasm.

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